REMARKS

Claims 1-33 are pending in the application.

Claims 15-33 have been rejected under 35 USC §103(a) as allegedly unpatentable over Tice, et al.. Applicants respectfully traverse this rejection.

Tice et al. is directed to the microencapsulation of a pharmaceutical agent of improved characteristics and higher quality, i.e. where the drug loading is not a limiting factor (col. 1, lines 48-60). Although Tice, et al. lists the active agent to be agricultural chemicals, perfumes, curing agents, dyes, oxidizing agents and biological agents, it provides no guidance on how to encapsulate a protein subunit without destroying its immunogenic properties and structure. The biological agents mentioned in Tice, et al. are contraceptive agents such as hormones and spermicidal compounds, gastrointestinal therapeutic agents such as aluminum hydroxide,...non steroidal antifertility agents, tranquilizers, vitamins, antimalarials, etc. The only mention of antigens are those to the microorganisms Neisseria gonorrhea, mycobacterium tuberculosis, Herpes virus, candida, and a few others at the top of column 6. There is no mention of encapsulation of a conformationally native subunit of chronic intracellular pathogen or more specifically, the microencapsulation of gp160 as required by the present claims. The only example of an active agent that was actually successfully encapsulated in Tice is progesterone. Since one of ordinary skill in the art could not predict whether gp 160 would be effective after microencapsulation without undue experimentation, it would not have been obvious from the teachings of Tice, et al. to use it in a microcapsule. Therefore, it is believed that this rejection is overcome.

Claims 15-33 have been rejected under 35 USC§103(a) as allegedly unpatentable over Cleland et al. Applicants respectfully traverse this rejection.

The present invention is directed to an immunostimulating composition comprising encapsulating microspheres, wherein the encapsulating microspheres are:

1) a poly(DL-lactide-co-glycolide) bulk matrix with
2) an immunogenic substance made of a conformationally native subunit of chronic intracellular pathogen, wherein said subunit is gp160, which in the course of natural infection with that pathogen, is exposed to the host immune system on the surface of free pathogen and/or pathogen-infected cells.

In other words, a protein subunit is presented to the immune system of a host via a microcapsule formulation. The protein subunit elicites an immune response in the host.

Cleland, et al. is directed to microencapsulation of antigens and has been cited by the Examiner for its disclosure of encapsulating HIV. Cleland, et al. does not disclose the microencapsulation of gp160. Cleland, et al. discloses the microencapsulation of rgp120. The protein rgp 120 in Cleland, et al. is substantially different than gp 160 in the claimed invention because gp 160 is much heavier and has conformational surface determinatives that are different than rgp 120. The subunit gp 160 provides a different immunity than rgp 120 as well. The present inventors found that gp160 prior to microencapsulation and following spontaneous release from PLG microspheres showed the two to be essentially indistinguishable in terms of their binding to CD4 and recognition by HIV-positive patient serum. This retention of conformation dependent binding shows that structure of the antigen is not appreciably altered by the microencapsulation process. Cleland, et al. does not suggest the microencapsulation of

gp 160 or that gp 160 would survive the microencapsulation process without altered structure. Therefore, Cleland, et al. would not have rendered the claims obvious and this rejection is believed overcome.

Reconsideration and allowance are respectfully requested.

Respectfully submitted,

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